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Original Research

Clinical effect of monocyte/high-density lipoprotein ratio on the prediction of bone metastases in patients with prostate cancer

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Abstract
Aim: This study aimed to determine the predictability of bone metastasis with a Monocyte/HDL-cholesterol ratio in prostate cancer patients.
Material and Methods: A comparison of monocyte/high-density lipoprotein in patients with and without prostate cancer was planned. Patients with hematological diseases and lipid metabolism disorders and those who were using lipid-lowering drugs were excluded from the study. Out of 95 patients, 54.7 % of the patients participating in the study were metastasized, while 45.3 % did not. Inflammatory markers with neutrophile-lymphocyte ratio (NLR) and thrombocyte-lymphocyte ratio (TLR) were found to be high in patients with bone metastases.
Results: Statistically significant difference was found between the patients' presence or absence of metastasis and NLR t (93) = 2.089; p = 0.040; p <0.05). Another statistically significant difference was observed between the non-metastasized patients and TLR (t (93) = 2.586; p =0.012; p <0.05).
Discussion: In the current study, there was no relationship found between the monocyte-HDL ratio (MHR), Gleason Score (GS) level, and bone metastasis. The relationship between monocyte metastasis and HDL-C metastasis cancer is controversial in the literature.

Keywords
Bone Metastasis, Prostate Cancer, Monocyte, Lipoprotein, HDL-Cholesterol

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Introduction

The development of atherosclerotic plaque, the biology of tumor formation and metastasis are linked to angiogenesis. Main molecular inflammatory pathways and their nuclear transcription factors such as NF kappa B, play an important role in the pathogenesis of both atherosclerosis and cancer. Altered expression of proteases associated with thrombolysis plays a role in atherosclerotic plaque progression and in the process of cancer invasion and metastasis [1-3]. The relationship between HDL-cholesterol and cancer incidence and mortality is controversial [4]. There are limited studies on directly affecting HDL-cholesterol levels and cancer mortality. Low HDL-cholesterol has been identified as a poor prognostic factor in many cancers [5]. A relationship has been found between low HDL-cholesterol levels and prostate cancer [6]. After monocytes enter the tissue, they can transform into tumor-associated macrophages. It has been found that breast and skin cancers play a role in the progression and metastasis myelomonocytic cells in mouse models [7]. Metastasis-associated macrophages cause tumor progression in metastasis [8]. Overactivation of monocytes can increase oxidative stress and increase inflammation. HDL-cholesterol has an impressive effect on monocyte migration by showing anti-inflammatory and antioxidant properties.

Monocyte/HDL-cholesterol has been used as an oxidative stress inflammation marker. HDL-cholesterol neutralizes the pro-inflammatory and pro-oxidant effects of monocytes by inhibiting the migration of macrophages and the oxidation of low-density lipoprotein cholesterol (LDL-C) molecules [9]. Therefore, features such as monocyte count (MHR) and HDL-cholesterol ratio may indicate the patient's inflammatory status. Consistent with this, the association between increased MHR and cases of atherosclerosis has been demonstrated. MHR has emerged as a new cardiovascular prognostic marker in previous studies.

Prostate cancer has a high mortality rate despite new treatment modalities. Inflammation is responsible for the etiopathogenesis and progression of many cancers. Monocyte/HDL-cholesterol is a marker of inflammation. Prostate cancer most commonly causes bone metastases. This study aimed to determine the predictability of bone metastasis with Monocyte/HDL-cholesterol ratio in prostate cancer patients.

Material and Methods

Sample Collection and Processing

Routinely checked blood lipid and hemogram profiles and PSA value, which are biochemical parameters, were scanned and recorded until 2017 June-October 2020. Data belong to patients aged over 18 years having histopathologically diagnosed prostate cancer. Prostate cancer bone metastasis was detected on a whole-body bone scan. Patients with hematological diseases, those using lipid-lowering drugs, and having lipid metabolism disorders were excluded from the study.

Statistical Analysis

A detailed statistical analysis was performed for the monocyte HDL ratio (MHR), neutrophile lymphocyte ratio (NLR), monocyte lymphocyte ratio (MLR), and thrombocyte lymphocyte ratio (TLR). Results are presented in the form of tables. Levene's test was applied where required.

Ethical permission

Ethical permission for this study has been granted by the Afyonkarahisar Health Sciences University, committee of clinical research ethics dated 02.04.2021 meeting number 2021/4 encoded 217-2011/KAEK-2. As seen in Table 3, there is no significant difference between the patients' metastasis status and the ratio of monocytes/HDL ($p=.752;p>0.05$) and ratios of monocytes/lymphocyte ($p=.065;p>0.05$). However, a statistically significant difference was determined between the patients' metastasis/non-metastasis status and the neutrophil/lymphocyte ratio ($t(93)=2.089$; $p=.040$; $p<0.05$). According to this result, it was observed that neutrophil/lymphocyte levels ($x=5.18$) of patients with metastasis of prostate cancer were higher than those in which prostate cancer did not metastasize ($x=3.33$). A statistically significant difference was determined between the patients' metastasis/non-metastasis status and the platelet/lymphocyte ratio ($t(93)=2.586;p=.012;p<0.05$). According to this result, it was seen that the platelet/lymphocyte levels ($x=251.36$) of the patients with metastasis of prostate cancer were higher than the patients without metastasis ($x=189.36$).

Results

As seen in Table 1, it was found that the disease metastasized in 54.7% of the patients participating in the study, while the disease did not metastasize in 45.3%. As seen in Table 2, there is no statistically significant relationship between the patients' metastasis/non-metastasis and monocyte/HDL-C, neutrophil/lymphocyte and monocyte/lymphocyte ratios. However, there is a statistically significant negative low-level correlation between the presence or absence of metastasis and the platelet/lymphocyte ratio. As seen in Table 3, there is no significant difference between the patients' metastasis status and the ratio of monocytes/HDL ($p=.752;p>0.05$) and ratios of monocytes/lymphocyte ($p=.065;p>0.05$). However, a statistically significant difference was determined between the patients' metastasis/non-metastasis status and the neutrophil/lymphocyte ratio ($t(93)=2.089$; $p=.040$; $p<0.05$). According to this result, it was observed that neutrophil/lymphocyte levels ($x=5.18$) of patients with metastasis of prostate cancer were higher than those in which prostate cancer did not metastasize ($x=3.33$). A statistically significant difference was determined between the patients' metastasis/non-metastasis status and the platelet/lymphocyte ratio ($t(93)=2.586;p=.012;p<0.05$). According to this result, it was seen that the platelet/lymphocyte levels ($x=251.36$) of the patients with metastasis of prostate cancer were higher than the patients without metastasis ($x=189.36$).

Table 1. Descriptive statistics for data

Status	Group	f	%
Presence of metastases	Yes	52	54,7
	No	43	45,3

n=95

Discussion

There was no statistically significant relationship found between

Table 2. Analysis of the correlation between the data and whether the disease metastasized

Variables		Metastasis present/no	Monocyte/HDL	Neutrophil/Lymphocyte	Monocyte/Lymphocyte	Platelet/Lymphocyte
Metastasis present/no	r	1				
	p					
Monocyte/HDL-C	r	-0,033	1			
	p	0,752				
Neutrophil/Lymphocyte	r	-0,202	-0,007	1		
	p	0,05	0,945			
Monocyte/Lymphocyte	r	-0,19	,256*	,700**	1	
	p	0,065	0,012	0		
Platelet/Lymphocyte	r	-,241*	-0,152	,720**	,677**	1
	p	0,019	0,142	0	0	

*p<0,05;p<0,01;n=95

Table 3. Analysis of the differences between data and the presence or absence of disease metastasis

Variables	Metastasis Status	Levene's Test							
		n	x	sd	F	p	t	df	p
Monocyte/HDL-C	Yes	52	0,01	0,01	0,846	0,36	0,317	93	0,752
	No	43	0,01	0,01					
Neutrophil/Lymphocyte	Yes	52	5,18	5,46	4,22	0,043	2,089	93	0,040*
	No	43	3,33	3,01					
Monocyte/Lymphocyte	Yes	52	0,49	0,27	2,852	0,095	1,87	93	0,065
	No	43	0,39	0,23					
Platelet/Lymphocyte	Yes	52	251,36	242,59	9,359	0,003	2,586	93	0,012*
	No	43	159,36	75,87					

*p<0,05;n=95

patients' metastasis as shown in Table 1. However, there was a statistically significant negative and low-level correlation between patients' metastasis with their thrombocyte/lymphocyte ratio. The inflammatory response has been linked to tumor metastasis and the survival effect in many cancers. Studies have determined that hematological parameters of cancer patients, including monocyte-neutrophil-platelet ratio, are associated with prognosis. Wang et al. showed that peripheral monocyte count predicts poor clinical results and aggressive tumor characteristics in patients with castration-resistant prostate cancer [CRPC] [10]. Similarly, Shigeta et al. has reported that high absolute monocyte counts predicted poor prognosis and aggressive tumor characteristics in CPRC patients [11]. In addition, the effect of immune cell ratio, such as the neutrophil/lymphocyte ratio [NLR], on the prognosis in gastric cancer has been reported [12]. In the study conducted by Ceyaln et al., bone metastasis has been predicted in high NLR prostate cancer [13]. In the study by Jing-Ya et al., higher NLR and PLR [platelet-lymphocyte ratio] were found in patients with higher bone metastasis [14]. In the current study, in accordance with these studies, inflammatory markers with NLR and PLR were found to be high in patients with bone metastasis.

Circulating monocytes play an important role in the metastasis process in prostate cancer [15]. An increase in the peripheral monocyte count and lymph node metastasis has also been increased [16]. In the current study, no difference was found in the MLR rate in both groups. However, in the study conducted by Azeb et al., peripheral monocyte count was not found to be associated with metastasis [17] that agrees with the results obtained in the current study.

No significant differences were found between metastasized and non-metastasized patients' data i.e., MHR (p = 0.752; p> 0.05), MLR (p = 0.065; p> 0.05). However, a statistically significant difference was found between the patients' presence or absence of metastasis and the neutrophil / lymphocyte ratio (t (93) = 2.089; p = 0.040; p <0.05). According to this result, it was observed that the neutrophil / lymphocyte levels [x = 5.18] of the metastasized patients were higher than in the patients whose prostate cancer did not metastasize [x= 3.33]. A statistically significant difference was determined between the non-metastasized patients and TLR [t [93] = 2.586; p =0.012; p <0.05]. According to this result, it was observed that the thrombocyte / lymphocyte levels [x = 251.36] of the metastasized patients were higher than the patients whose prostate cancer did not metastasize [x = 189.36].

Abnormal lipid metabolism is being investigated as one of the important mechanisms in carcinogenesis. As a result of defects in lipid and lipoprotein metabolism, metabolic syndrome and obesity have been found to affect cancer risk and prognosis [18, 19].

High- and low-density serum lipoproteins have been found to act as key lipoprotein transporters of cholesterol to cancer cells through receptor-mediated mechanisms. Low LDL-C has been shown in some studies associated with a higher risk of malignancy.

Some studies have found a relationship between HDL-C and cancer incidence. It may contribute to tumor progression [20]. There is a positive association between low HDL-C and breast cancer risk in postmenopausal breast cancer [21]. Pre-treatment low HDL-C levels were found to be associated with

poor prognosis in non-small-cell lung carcinoma.

Epidemiological studies of the relationship between HDL-C and the prostate are contradictory. While some studies present a relationship, others deny it [22,23]. HDL-C prostate cancer risk and disease severity are controversial in the literature.

Low HDL-C and high triglycerides were found to be associated with higher grade in prostate cancer [24]. In conclusion, the hypothesis of this study was to determine the effect of MHR used as an inflammatory marker on predicting bone metastasis. Also, the association between increased MHR and cases of atherosclerosis has been demonstrated. MHR has emerged as a new cardiovascular prognostic marker in the previous studies [25]. There are limited studies in the literature on the MHR in cancer. It was found to be high in differentiated thyroid cancer. The relationship between monocyte metastasis and HDL-C metastasis cancer is controversial in the literature. There is a need to expand this study on a large scale by increasing the number of patients.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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